

THESIS  
on  
Friedreich's Ataxia.  
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A short treatise on Friedreich's ataxia,  
with a discussion of the classic symptoms,  
a short digest of the more important patho-  
logical points, differential diagnosis,  
theories with regard to causation, prognosis  
and treatment. An account of two hitherto  
unpublished cases is added together with  
a short Bibliography by W. Alexander Gibb.

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It was in the year 1861 in the month of September when Friedreich first read a paper on this subject before the Congress of German naturalists and physicians at Spire, ,that this disease came under the attention of the Medical World. The eminent observer of Heidelberg had for a year or two previously very carefully noted several cases of progressive locomotor ataxia, in which Duchenne of Boulogne by his paper on the subject ~~having~~ aroused great general interest . Friedreich had frequent opportunities of consulting with, and showing his cases to friends, such as Eisenmann, Hasse, Kussmaul and Virchow and he differed from the general studies of Duchenne, and with them, concerning his cases. The cases which had come under the observation of the great clinician, did indeed differ from these now classic types , and he was right to put them in a different class: though for some considerable time they were considered even by him to be but anomalous types of one class . The rather ingenious theory put forward by him was " that in the different cases of locomotor ataxia published , we find sometimes sensory disturbances sometimes complete absence of them , it is because in the first case degeneration of the medullary fibres is not limited to the posterior columns, it has invaded other regions of the spinal cord". He had the opportunity of doing three autopsies on these cases. Still it was some considerable time before hereditary ataxia was recognised as a special disease. Charcot first recognised it as a special affection in

the year 1884, when he lectured upon, and shewed a patient suffering from this complaint to his clinique at the Saltpetriere. The first mention of this affection in England occurred in 1871, when Dr. Carpenter of, Croydon brought before the clinical society of London two cases which were not at the time recognized. On the 8th. Oct. 1880 Dr. Gowers shewed to the same society three cases belonging to a family of nine of whom five were ataxic. From this time onwards from time to time cases have been reported, and the disease written and commented upon until its literature alone has become considerable. Still it is far from being a common form of nervous disease.

Friedreich's ataxia as I think we may term it, forms one of a group of (family) affections well known to the neurologist. Londe (1) in his very interesting monograph on "heredo-ataxie-cerebelleuse" another of the group of familial disease, and one which we will consider later on with regard to Friedreich's ataxia, has given a very good definition of a family disease.

#### Definition of a family disease.

"By a family disease we are to understand one which tends to attack many members of the same stock, and particularly it would appear members belonging to the same generation and which depends not so much on extrinsic causes, whether these be intrauterine or subsequent to birth, as upon a fault inherent in the germ or introduced into it by procreation"



To proceed, Friedreich's ataxia is a chronic inflammatory degeneration of the spinal cord, developing generally in infancy or childhood, in cases where there has probably been an arrest of development of the cord during foetal life: this being frequently the result of hereditary predisposition.

The lesions are situated chiefly in the posterior columns, the lateral and cerebellar tracts and the columns of Clarke, other parts of the white and gray matter may be affected, and the sclerosis extends slightly into the medulla.

Clinically the affection is characterised by a disturbance of coordination of the bodily movements, developing gradually from below upwards, and eventually affecting speech.

A peculiar form of talipes, curvatures of the spine, and nystagmus are usual. Kneejerks are nearly always absent. Paralysis and slight disturbances of sensation are occasionally met with in advanced cases. Affections of the visceral, vasomotor, or trophic systems are very unusual, and the mental condition is unimpaired.

Recorded instances of the direct transmission from father to son both being ataxic are rare; generally it skips a generation. Vizioli (2) reports one case noted below. Everett Smith (3) describes another case.

Neuropathies, alcoholism, consanguinity, all appear to exercise some influence as factors in the production of hereditary ataxia. There is no question of alcoholism exercising <sup>ing</sup> some influence, as it is one of the commonest family histories we find. The question of alcoholic conception being an important one. Friedreich laid great stress on this

and though Griffiths (5). disagrees with him, still there is a distinct weight of evidence in favour of the theory

( Friedreich's cases 6 out of nine.)

(Bramwell's(4) cases and others )

Tuberculosis and syphilis apparently have no influence. Cardiac affections are said to have some influence . The influence of acute disease upon cases is very great as a rule the symptoms of the nervous affection coming on directly after recovery from the acute illness, the disease often making rapid strides after such. With regard to ataxic histories I append three interesting histories of ataxic families at the end of the treatise.

We will now proceed with the history of the two cases which present most of the classic symptoms: after which the symptoms, Differential diagnosis, pathology, and theories with regard to causation, will be discussed.

Two cases of Friedreich's ataxia which <sup>were</sup> under my own personal observation for some months hitherto unpublished; the cases of Wm. and Minnie Harding.

I first saw Wm. Harding in the out-patient department of the Gloucester General Infirmary. His mother having brought him with a view of seeing what could be done for him , as his walking had been getting bad . Being struck with the peculiar movements in the boy's head, body, and speech; the fact being also elicited, that his walking had never been very good , I admitted him as an in-patient on the 1st. Feb. 1897.

#### FAMILY HISTORY.

Parents were natives of, and had resided in Gloucestershire

all their lives . they were both alive, strong, and healthy. His father is a collier . There were six in the family, one brother and a sister died in the Hospital in childhood, not known from what they suffered. Two brothers at home well and strong one aetat 10, the other four years . There is also one sister at home who is said to be worse than her brother aetat. 12 years. There appears to be no family history per se which can be gathered. There is no history of alcoholism or syphilis on the part of the parents . No phthisis. With regard to their relations there is no history ~~no~~ history of insanity of fits, or nervous disease can be obtained. Circumstances seem to have been poor <sup>but</sup> not exactly poverty stricken.

The family of six consists as follows:-

(a)	One brother	Aet. 17	<u>Ataxic</u>
(b)	One sister	Aet 12	<u>Ataxic</u>
(c)	One brother	Aet 10	<u>healthy</u>
(d)	One brother	Aet. 4	healthy
(e)	one brother	(not known) died in hos-	
(f)	One sister	" "	pital in child- hood

#### Case one

William Harding - no occupation - Gloucestershire aet 17

#### Patients History

The history in this case was very vague and exceptionally difficult to elicit . He remembers that he had an illness when two years old, but does not know what it was, it was



however severe. He was like other children of eight years old, <sup>up to</sup> then he thinks he has scarlet fever, but he is not very sure about it; When about 12 years old he suffered from dropsy. His mother however noticed that when he was about eight years old he was not quite as nimble on his feet as he had been, and that he frequently fell down and hurt himself. However no very great attention was paid to this at the time, things went on very much as before until he was twelve years of age, when as was seen above he suffered from dropsy. The history was very vague, both he and his mother strongly asserted that he had a very severe illness at that time and when he got about again a very great change was noticed in his manner of walking, long after his general health had been regained, his walking not only got no better but even worse than before. His mother too thought that there seemed to be a little dullness and a delay in answering questions. Things had continued very much in the same way getting if anything a little worse. He could not be put to work, but he did a little in the way of frightening birds off the fields for farmers. He often stumbled about, and was very clumsy in his ways.

#### Present Condition.

Medium height. Dark hair. Good teeth. Muscular development very fair, Mouth kept a little open. Lips a trifle thick., Does not look very intelligent to a superficial glance. Temperature 98.4. Attitude. Does not sit upright, when he walks about he shambles along.

#### Alimentary System

Appetite good, teeth very good. Tongue clean and



fairly steady on protrusion. No pain after meals, no waterbrash, no sickness. Bowels regular. Micturition regular. No incontinents.

Respiratory System

Integumentary system

Nil

Circulatory system

Urinary system

Nervous system.

The following conditions are to be noted on the motor side. When sitting still very slight movements on the upper part of his body and trunk took place and these seemed to be quite involuntary. He can keep his hands quite still if told to do so but the movements come on gradually after a while. When standing, he is inclined to sway a little from side to side, he keeps his feet a little apart, quite enough to be just noticeable.

He is very clumsy in turning, when asked to come quickly round any place such as the corner of the bed &c. he is almost certain to either catch against the corner and have to steady himself by putting his hand on the bed, or will blunder against the corner, just grazing it. With his boots off I think he is distinctly worse as he does not seem to have anything to grasp with his feet. (I will refer to this later). If told to stand with both feet together he will do so for a minute, but the movements of the head and the trunk are very much increased; after about a minute's time he will probably fall. If told to shut his eyes and

keep his feet together he will do so for a shorter time than before, but he can do so, though the time is very short appreciably. He stumbles over at once if told to stand on one leg. He does all his movements very much better if he has his boots on, the weight of his boots appearing to help him to a certain extent.

A thing one particularly notices with the patient is that he never keeps his head upright. It is very interesting to watch the muscles of his ankles and calf when he is trying to stand upright, they seem to be in a state of intense contraction, the tendo Achilles specially so, far more so than one would imagine necessary to control his equilibrium. His gait is very characteristic of his disease, he puts his feet down with a bang, he does not do this from spasm, but simply because his coordination is defective. He appears to shamble along as if both his joints were loose at the knee; and when he wore heavy boots, the weight of the boots apparently increasing the play of his feet, but for all that they seemed to give him some support. If asked to turn he did so very awkwardly, he never turned smartly, however, if told to halt he did so quickly. He could do everything in the way of voluntary action, could lace his boots after a fashion, took a long time over it; could unbutton and button his coat and vest with his fingers, he had some difficulty with the smaller buttons, still he could just manage to do it. There was also a certain amount of hesitation about the movements of his fingers. He could pick up a penny off a book but he did it in a very curious way, he never picked it clean off but rested his hand on the book first

All these acts seemed to increase the peculiar movements of his hands; in fact the word choreiform describes them admirably. It was most peculiar when told to pick up anything from the bed, such as a pencil, a thermometer case &c. without touching the bed first, his hands seemed to circle about in the air first and then dart down to pick it up, however, he frequently failed to do even this. On reference to other authors I find that these movements, called "hovering" by some, are very well described by Charcot (9) but he describes the movement as an analogous to the circling swoop of a bird of prey. "Perhaps this is more poetic than scientific". As regards feeding himself he can do so very well. He can carry a cup if not too full, to the mouth and drink the fluid completely without these choreiform movements being increased. His head during all these movements being swayed from side to side, a certain nodding movement being superadded. This symptom of his was typical of what M. Paul Bloc (8) wrote "La tete oscille, comme celle d'une personne assise en train de s'endormir". If asked to touch his nose when his eyes are shut he is not very accurate, not, perhaps touching his nose more than twice out of three attempts there is a certain amount of uncertainty in his finger movements. When in bed he can do things very much better if allowed to rest his arms.

#### Involuntary Movements.

The involuntary swaying of head and trunk before noticed. Very slight twitchings of the face occur and es-

pecially of the mouth. There is slight lateral nystagmus when patient is told to look to the right or left. This occurs in both eyes. No horizontal nystagmus was observed. When the tongue was protruded it was ~~fai~~<sup>l</sup>ly steady but if the protrusion was kept up for a little time, very fine fibrillary twitchings were to be observed in it.

#### Disturbance of Speech

This is markedly affected. The boy speaks and looks as if he were <sup>half</sup>~~fast~~ asleep but it is not that he is dull for he is really a very intelligent boy, in fact superior to youths of his class. He does not seem to have sufficient power over the muscles of articulation. He speaks in a curious hesitating manner, which on first hearing gives one the impression that one is listening to the "staccato" speech of a disseminated sclerosis, but there was no definite stoppage, there was a <sup>slurring</sup> over of words that stopped short at that, apart from the fact that <sup>the</sup> tones differed; it was also as unlike as possible the explosive sentences of Marie's type of case. He gave one the impression that he was speaking thickly as a result of too much liquor: there was however always a marked deliberation in his manner of speaking. Of course one had to make a certain allowance for the differences in dialect, but, even making allowance for that there was still a marked change. I never heard him speak in any other way during the whole time he was under my observation. The voice was not reedy but of a fair calibre, it was very monotonous to listen to. He read a book in the



same monotonous way, he would thus read November, as if it were Noavembrrrrr no, Sir, noaasurrrrr. The whole speech never varied, always the same hesitating slurring utterance. He could write a little, not very well, but still readable.

#### SENSORY FUNCTIONS.

He is not giddy: but he at times suffers from a kind of bilious vertigo which passes off in a few hours or less.

No abnormal sensation, no formication etc.

#### Tactile Sensations.

There was no loss of time in referring to tactile impressions. Sensibility to heat and cold fair. (N. B. This seemed to vary sometimes but was always very fair)

Tests with the aesthesiometer were normal.

Sense of weight. Very fair.

Muscular sense. Very good.

Muscular Power. Is fair.

Hearing. Very acute.

Sight. Very good.

Eyes. The pupils react both to light and accommodation, no mydriasis, no scotoma. or ophthalmoscopic exam .

(a) "The veins were normal in size and colour

(b) The disc was perfectly normal there, was no flattening, nor was it unduly pale.

Superficial Reflexes. present

Taste. Normal. deglutition defaecation and mic /uriton are normal

Patellar Reflexes. Absent on both sides ( though on one or two occasions I obtained at first a slight tremor onpercussion on the left side, this went latterly)

No ankle clonus . Speaking generally no trophic influence was wanting.

Condition of muscles and deformity.

His muscles are not flabby but fairly developped . Hands are normal, grasp of the hands excellent. He can shut up his hand, flex and extend his wrist and fingers very well; the clumsy way he picks up things only being due to the faulty coordination of his muscles. He can separate his fingers etc. he can flex and extend his phalanges.

The feet show some slight changes. On standing one notices that his calf muscles and the tendo achilles appear to be in a state of contraction, but there is almost a tendency to flat foot and that the great toe is very prominent, it approaching the middle line of the foot too closely . One notices also that the scaphoid bone on both sides is prominent . When the boy lies in bed you notice that the arch of the foot appears to come back, that the dorsum is more prominent and that the extensor long :hallucis is inclined to be contracted, drawing the big toe up.

The boy sits in a chair as if he had some scoliosis, but none

could be detected, though he occupied the typical attitudes when he was up, for one to develop it

Electrical Reactions Practically Normal ( Faradic & Galvanic Currents)

### Case 2.

The case of Minnie Harding aet. 12.

The younger sister of the previous case. During my examination of her brother I elicited the fact that he had a sister at home who suffered in much the same way as he had done but was very much worse. I sent for the sister and admitted her as an in-patient March 22nd. 1897. Her history was as follows :- She had always been a strong child and was like other children up till 5 years ago ( aet 7). At that time she had an attack of measles and after that her legs began to get weak, and she sometimes fell; her mother said that though very willing she was not at all nimble. She has continued going to school up to twelve months ago. Her legs had got very much wasted and she could not get about, in fact had to be carried.

Present Condition.

Fairly intelligent looking. Neuro-rheumatic type. Flush on each cheek, good colour, black thick coarse hair. Brown eyes. Lips a good colour. Good teeth, large and flat. Temperature 98.4. F.

Past Illness.

Simple childish ailments, nothing important, she had measles when 7 years old. No scarlet fever

Respiratory System. Practically nil. There is some dullness in the sub clavicular regions anteriorly on both sides. On auscultation harsh and purile breathing. Vocal resonance a little increased. Vocal fremitus nil.

Circulatory System. All cardiac sounds normal and closed.

Locomotor System. Arms muscles poorly developed, although what there is is pretty good. Grasp fair. There is some flattening of the muscles of the thumb on both sides: patient have says that her hands got smaller and flatter.

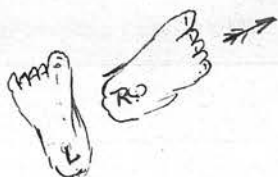
Legs. Muscles are wasted. The extensors appear to have the most power. The extensor longus hallucis in a state of contraction in both feet, this was noticed early.

#### NERVOUS SYSTEM.

When sitting a slight swaying of the body takes place this is not very noticeable except when the patient is made to sit up in a hard chair, as a rule the patient sits in a basket chair propped up and wedged in with cushions. She cannot stand by herself and cannot walk. She can sit up for a little while by herself but soon falls back in the chair. During the time she is sitting up the whole body seems to sway and her head falls forward. The choreiform movements are not so marked in her case as in her brothers. Her gait is very peculiar, she cannot walk by herself, but if held up on either side she can take a few steps. It is most peculiar to observe her feet, as before noted the extensors longus hallucis on either side are in a state of contraction the dorsum of the foot is prominent and the arch is greater than normal.



Both feet are alike, now when she attempts to walk the extensors of the leg are thrown into action and, being very much more powerful than one would suppose to look at the wasted condition of the legs. Now one notices that the prominent arch disappears and the foot becomes almost flat. In her particular case as she totters along one notices that the feet are everted slightly, on the inner side of the foot so that the external border of the foot becomes superior, looking upwards and outwards. One notices too that she places one foot behind the other closely as if for support thus -



(Musso speaks of the gait in some cases as exhibiting the lateral projection of the feet as compared with the forward propulsion seen in Tabes). It is also curious to note the peculiar movements of the extensor tendons of the toes when placing the feet on the ground; Before the toes finally take a firm hold of the ground a curious hesitating movement takes place which is called by some "le danse des tendons". She is not nearly so awkward as her brother in picking up things with her fingers, she certainly cannot thread a needle with cotton, but she can knit a little, can button some of her clothes but soon gets exhausted. She can drink out of a cup without spilling any of the fluid if the cup is not too full. She does all these things in a curiously "ataxic" way. When told to touch her nose with the tip of her finger with her eyes shut, she can do this; there appearing to be only

a slight hesitation when the finger is nearing the tip.

There are practically no choreiform movements of the face but her head was moved in the usual swaying manner.

Her tongue when protruded was fairly steady but showed the fine twitchings seen in her brother's case. She sleeps very well, no movements are to be noticed during her sleep. Involuntary movements of the eyes are seen when told to look at an object to either the right or left, when a slight lateral nystagmus occurs. There is no horizontal nystagmus. Taken on the whole her speech is very fair, at times when she is a little excited one hears the slurring of words. She is a nervous child and talks very little even to the nurses. Writing is not good but she can read a little: Now one is struck by the monotonous slurring speech which is so characteristic when she reads.

#### Sensory Functions.

No giddy feelings, no bilious vertigo. Tactile sensations good. She can refer tactile impressions very accurately. Sensation to pain is very much dulled one can stick a pin half way into her leg without causing her any uneasiness, though there is no hesitation in referring a mere tactile sensation. Sensation to heat and cold very poor in the lower limbs. She cannot differentiate between hot and cold. (This curiously enough seems to vary a little from time to time but is generally very poor). These sensations in the arms and body are normal. No cloni can be obtained either in the upper or lower limbs. Muscular sense good in the arms.

but not very good in the legs , still she has some, though the perception is not very fine.

Hearing sight and taste good.

Deglutition , Micturition, Defaecation normal. Has never menstruated . Superficial reflexes. Normal.

Patellar reflexes quite gone on both sides.

Eyes. Pupils react to light and accomodation

Ophthalmoscopic exam

Nil ( a ) Arteries normal

( b ) Disc Normal

The nystagnus before noted

Condition of muscle and deformities.

The feet have been noted above (pescavus) on both sides. There is wasting of the muscles of the lower limbs the general muscular development is poor. There is a lateral scoliosis present; it is not very marked but still is quite distinct ~~and~~ the patient sits up . It is convex to the left in the upper dorsal regions andconvex to the right in the lower lumbar regions the head is bent forward a little . Electrical reactions were unsatisfactory.



Further remarks on the cases conjointly.

I had these two cases under my own personal observation for nearly three months , when unfortunately they had to make room for more urgent cases and since then have been lost sight of. I examined them at frequent intervals and never found any difference (The only minor one) perhaps being the slight tremors I noticed on examining William Hardings kneejerks (during the 1st. two examinations). They were mentally rather intelligent, though at first sight they both looked intensely stupid . The temperature never rose: they had both good appetites. Their condition did not improve at all; their general health was excellent and this is a fact which struck everyone that examined them. I exhibited, Arsenic, Iron , Strychnine, silver, Potassium iodide and other drugs but must confess that therapeutically not the slightest effect was produced. The use of the Battery was continued with the sister for some time and she said she thought that the battery "steadied" her. But personally I could not see the slightest improvement. They never suffered from lightening pains, there were no athetoid movements of the fingers and hands described by some observers. It may be interesting to tabulate briefly the two cases and then to discuss the symptoms



## Case 1.

## Family character.

1. Onset after a severe illness, scarlet fever 8 years.
2. First symptoms difficulty in walking
3. Slow advance of ataxia
4. Slight change in speech.
5. Increasing ataxia of body often falls.
6. Nystagmus.
7. Absence of kneejerks.
8. Slight tendency to Pes Cavus.
9. Intelligence, Sensory functions, Visceral functions, pupil reflexes, Normal.

## Case 2.

## Family character.

- Onset after measles, aet. 7.
- First symptoms difficulty in walking.
- Slow advance of ataxia.
- Nil.
- Marked ataxia of feet and legs could not walk.
- Nystagmus.
- Absence of kneejerks.
- Marked Pes Cavus and flattening of the muscles of the thumb.

Ditto.

Remarks on some of the more important symptoms

The first great symptom that strikes one when viewing either of the cases, or reading the histories of cases of this class of disease, is the disturbance of the motor system. Of the ataxia one may point out two forms.

1. Locomotory ataxia, or the ataxia associated with voluntary movement.
2. Static ataxia.

To add something further, we notice the tremulous jerky movement, which may be called choreiform movements, tremors

of the muscles of the tongue, of the face, so much so that articulation may be interfered with; nystagmus these are all evidence of a wide spread motor disturbance. Latterly certain muscles become paralysed.

# 1. ATAXIA associated with voluntary movement

This may be well seen as the patient walks or tries to walk. It was well seen in the first case, he kept his feet a little apart, his head bent slightly forward, his back bent. Then in his gait, one notices that he puts his feet down with a bang; first his foot hesitates a moment when put down, then the toes as it were feel the ground, and then the heels come down with a crash on the floor. He walked fairly straight but not absolutely so. He was inclined to walk putting a certain amount of lateral movement into his legs. He reels a little, more so after he has been sitting down, he appears to improve a little after walking. His steps are not equal. He appears to use his hands and arms to balance himself, and he keeps his eyes fixed on the floor a little in front of him. In locomotor ataxia, the gait differs from the former, though there may be some resemblance at some time in this form of disease. There is more exaggeration of movement the feet are raised higher and are brought down with more noise and perhaps decision than in Friedreich's disease. In locomotor ataxia the patient can walk in a straight line. In Friedreich's disease he cannot, he walks from side to side, you are afraid that he will stumble and fall

in fact he appears to be trying to overtake his "centre of gravity". It is as well to note that the gait of Friedreich's disease is "cerebellar" in type, and this is important from a diagnostic point of view. Thus at first ~~gives~~ <sup>has</sup> one the impression looking at the gait that it might be any one of the following. Marie's disease (10) disseminated sclerosis, or cerebellar disease. But added to the cerebellar gait, we may add other symptoms, especially when the patient stands still these may be traced in the trunk and extremities of the patient. They are called by Friedreich (11) static ataxia.

## 2. STATIC ATAXIA.

These movements were very well shown in both cases; when William Harding was standing still the muscles of his body were in a continual state of contracting. He stands with his feet apart, his feet clutching the floor, the tendons of the leg in a state of over-contraction. His head bent forward, his body slightly bent forward and slow swaying movements of the whole body occurred. The same thing occurred with his sister only if anything a little more marked. When she was sitting still one could hardly notice the movements. All the movements of the limbs could be increased by movement in both cases, such as picking up a small object off any place i.e. a penny, threading a needle, taking a cup of water and drinking it, buttoning her clothes etc.. If the patient be stripped you will notice that every muscle that is easily visible to the eye is in a state of movement in the effort to keep the erect position. In all the freer movements that as it were



were out of the way, one especially noticed the clumsy way in which they were performed. (Also it is well to note how helpful to the patients is the fact of their lying in bed, and how much better they perform some of the movements e.g. those for the feet, when doing so). Asking the patients to walk about with their eyes shut ( Romberg's test) is very valuable,

for diagnostic purposes but is of little use in this disease. Increase of unsteadiness with the eyes shut is often absent in Friedreich's disease, though in my first case it appeared to make him slightly unsteadier, still was not very marked. We may here class the symptom which is almost invariably present (not in all - Gowers 12 ) I refer to the nystagmus; this is perhaps best stated when taken in connection with the above. It is not a true rythmical nystagmus.

It has to be looked for with care and may be overlooked.

The method of observing is as follows:- Cause the patient to fix his eye either close to his nose, or the farthest object possible to the extreme right or left. The symptom is frequently late. It is well shown in both cases.

There is no nystagmus in the vertical plane. When the tension of the muscles of the eye ball are thus increased, distinct jerkings are seen, which may vary in rate and regularity. It is a sign not always easy to elicit

"Geigels cases" (13) " Mendel's" (14). Occasionally nystagmoid jerkings are found in those in weak health and even at times in the healthy. "Mackie White's cases" (15),

Ausschlag (16a) investigated 200 cases only 25 of which



showed no tremor, but the cases were unselected. In locomotor ataxia it is very uncommon, so that to a certain extent this may be a help in diagnosis. The tremors of the tongue which may be seen, when it is protruded from the mouth, we may refer to the same: beside the swaying movements, there are irregular movements, which are markedly involuntary and jerky in character, they have been called choreiform and are not so constant or so violent as in chorea.

Twitchings of the muscles of the face. These were noted especially in case 1. , not so marked in the sister. The head in both cases has a constant swaying nodding movement more marked in case 1. These movements are generally present in Friedreich's disease, and are a very important diagnostic symptom, occasionally they have even been mistaken for chorea especially marked was Zabloudowski's (16b) case. Painful cramps are mentioned by some as occurring in the legs at night. Besold's case (17) Bramwell case 1 Atl. 1. p. 46. Mackie Whyte's case (4).

Nocturnal restlessness has been noted by some, (Bramwell).

Athetoid movements occur too in a small degree, these have been reported by several observers as occurring in the hands

(Griffith's Case.). Athetoid movements of the feet and toes in walking (Ladame's 18, Wallace Anderson's cases). But in some of the other cases where these movements took place in a marked degree there were other features beside, which were uncommon and which would raise grave doubts as to whether they should be classed with Friedreich's disease ; notably Chauffard's (20) case and two other cases reported by Londe and Lagrange (21).

Of course there was in the case of William Harding a very slight amount of athetoid movement before his toes were placed on the ground.

#### DEFORMITIES

(a) (a) The hands (b) the feet (c) the spine

These are generally speaking uncommon, Griffith 's (The American Journal of Med:Sciences 1888(p 377 ) describes one of his cases " as having grasp strong but claw-like," and another as having claw-like hands .

"The hands were claw-like and one case had wristdrop " (Rook 22). One of Taylor's cases had difficulty in extension. Bramwell puts on record a family of three with the "claw-hand " Mackie Whyte also describes" that in three out of the four cases he has put on record, the attempt to extend fingers in line with the forearm at once brings out a more or less pronounced main en griffe." I will briefly run over the more important changes which were noticed in case two of the series he has published. When the hand is passive nothing is noticed. When told to straighten his fingers, flexion is produced at the wrist with some bending toward the ulnar side. The near phalanges are over extended in the four inner digits more so in the fifth than the fourth, in the fourth than the third and so on. The middle phalanges are flexed, and the terminals are nearly in a line with these. With regard to the joints the deformity is more marked in the inner than the outer digits. The fingers are separated a little from one another, the thumb is simply bent back. The more strongly the patient tries to

straighten the fingers the greater does the alteration in form become. The common extensor digitorum tendons can be seen standing out on the back of the hand and can be traced up the lower third of the forearm. The palmaris longus tendon too stands out prominently. The fingers can be abducted and adducted but to a less extent than normal. What is the mechanism of these conditions? The proper flexors and extensors of the wrist are all right for when the hand is closed:

Flexion and extension, abduction and adduction of the wrist occur normally. It is not a paresis of the ext. comm. dig. tendons (Duchenne's extensors of the near phalanges), for they are inserted chiefly into the near ends of the near phalanges.

So far from their being failure, or power to act, it appears to be the reverse, over action or over extension.

Mackay Whyte considers it to be due to a paresis, not paralysis of the interossei (though in time it may become this). The interossei flex the first phalanges, extend the second and third, and they also abduct and adduct the fingers. When they are weakened, and when the common extensor is thrown into action, the fingers assume the position above described. To keep the first phalanx in a line with the metacarpals, antagonistic action of its flexor and extensor is needed. Now note what Duchenne (Sydenham Soc. trans. 265) says "When the interossei fails, the unopposed extensor causes an exaggerated extension of the near phalanges, and the extension of the middle and far phalanges do not only not occur, but are on the contrary flexed in direct proportion to the degree of extension of the near phalanges".



The flexion at the wrist may thus be explained.

When the hand is extended not only the proper muscles of the wrist act together, but also the long extensors and flexors of the fingers. The combined effect of this action placed the metacarpals on a line with the forearm. Now if the interossei are weakened, and the near phalanges are over-extended, the balance is upset, the common extensor acts at a disadvantage as regards its extending action on the wrist and there is an appearance of slight wristdrop. The great amount of distortion in the ring and ulnar fingers corresponds with the condition of the injury of the ulnar nerve, and is accounted for by the escape of the first two lumbricals which are supplied by a branch of the median nerve. That the whole terminal part of the ulnar is not affected, is proved by the intact sensibility, among other points.

One must bear in mind these points when one comes to consider the condition of deformity in the foot. It is interesting to have so complete a description of the main engriffe deformity in Friedreich's disease, when as we have seen it is an unusual symptom. None of the two cases, whose histories are shown here had any symptoms of the kind. The only one being in case 2 where there was slight flattening of the muscles of the thumb. There was no contraction of any kind.

#### (b) The feet

Here we have well marked deformities of the feet. The deformities which we were about to describe are very characteristic of Friedreich's disease. They are by no means an



essential symptom. "Griffith's out of 143 cases found only 27 who were deformed".

In Rutimeyers families of Blattner and Kern described elsewhere, prominence of the extensor proprius hallucis was regarded as a very bad sign and was an early one .

Ladame lays great emphasis on this in his monograph.

In case 2 this has been noticed, there is a contraction of the extensor longus hallucis. In several cases on record these deformities are well marked, and in one or two were among the first symptoms noticed. This is uncommon. Briefly

"Baskett's case(23) a girl of 13½ was an hospital patient for double talipes varus at 8½ years. Her symptoms began at 6. But usually these symptoms are later in coming on . Here we might note among well marked cases those of Dr. Mackey Whyte's cases 2 and 3, and some cases described by Dr Byrom Bramwell Atlas 1. p.39, a case of Dr. Mackay of Devizes, Ladame's cases and Everett Smith. In the case of the Hardings as before

mentioned it was more marked in the sister than in the brother.

Briefly the characteristic deformity of Friedreich's disease appears to be a condition of pes cavus or hollow claw-foot.

A general glance at the foot in a typical case gives one the idea that it is smaller and stumpier (The best way to observe the condition is when the patient is sitting on a chair and the feet are raised from the ground) The dorsum of the foot appeared to be more prominent and the foot more arched, the balls of the toes especially <sup>of</sup> the great toe appear to be enlarged.

The first phalanges of the toes especially of the great toe are over-extended on the metacarpal bones. The extensor tendons especially the extensor prop:hallucis stand prominently out. In some cases there may be a little purpleish colour observed about the feet and they are frequently cold.

When the patient stands the conditions are much less marked, The shortening, the arching and the prominent instep all disappear. Still even on standing, the extension of the first phalanx, and the prominent extensor tendons show out.

This deformity is usually well developed at a comparatively early date though not an early symptom, and is a very important diagnostic symptom.

How is it caused?

Is it in the same manner, that main en griffe occurs in the hand? . It may be so, and may therefore be due to a weakening of the interossei of the foot ( including as well the short flexor and abductor of the great toe). There may certainly be a real weakening of the antero-lateral muscles of the leg. in a good many of the cases there is certainly retraction of the calf muscles and tightening up of the tendo achilles Vide case 1 & 2. It is certainly a very ingenious theory and one which must be weighed carefully, but still it is curious that more cases of the hand deformity do not occur, for why should the plantar be selected <sup>rather than</sup> and the palmar interossei? The more generally received opinion is that it is a condition of paralytic club-foot and it is caused according to some authorities by the lesion of the crossed pyramidal tract in the lateral columns of the cord.

With regard to the affection of the lateral columns I think that an extract from a paper on "~~the~~ investigation "into the plantar reflex." by Dr. Collier (24) will be interesting.

He examined six cases of Friedreich's disease for this sign.

All six cases showed a marked extensor response . Four of the cases had marked pes cavus and absent kneejerks, two had slight pes cavus and the kneejerks were just obtainable, Clinically the only sign of the affection of the lateral columns is the extensor response in the plantar reflex, and pes cavus.

Further it is interesting to note, he writes "I have also had the opportunity of examining four cases of early Friedreich's disease with commencing pes cavus; in all these cases the earliest sign of deformity was the retraction of the big toe, and the second sign of note the spasm of the tibialis posticus and peroneus longus muscles, as evidenced by the constant standing out of their tendons behind the internal and external malleoli respectively!" Note " He considers, <sup>that the opinion</sup> that pes cavus of spastic conditions being due to weakness of the interossei, is not justified." In both the cases reported there is presented very much the conditions described above. The big toe drawn up, the clawing of the extensor tendons, the prominent dorsum, the large arch, the contractions of the posterior group of muscles and tendo achilles.



## SPINE DEFORMITIES.

Curvature of the Spine in this complaint is of very common occurrence. Soca says it occurs in half number of cases. It may be lateral or antro-posterior or may occur in both ways.

In the common form of lateral curvature in young people, the main dorsal convexity is usually an exaggeration of the natural curve to the right and this frequently occurs. In the first case there was no lateral curvature present, but it is extremely probable that he will develop one very shortly, as he is always in the best position to develop it. His sister has left lateral curvature, with a tendency to kyphosis, in fact they both have a tendency that way and I should think that it is only a matter of time before that is developed also. Hallion (25) in his article upon spinal curvature in nervous disease asked the pertinent question "Are nervous lesions capable of causing an alteration in bones and especially of the vertebrae?"

Soca considers that muscular weakness is alone quite sufficient to account for the condition.

## CONDITION OF THE SENSORY SYSTEM.

Sensibility of the skin. This may be quite normal but nevertheless it is not uncommon to find a slight dulness. In case 1 the condition is practically normal. In case 2 we find some differences. There is no hesitation in referring mere tactile sensation, but there is very little sensibility to pain, and the thermal conditions and tests generally. It curiously enough appears to vary at times, and is at times better than others



Contrast with this Mackay Whyte's case 2. who had analgesia and then apparently regained sensibility. It is interesting to note here the condition in three cases recorded by Klippel and Durante "by Londe". These were some cases selected by Marie for his type, heredo-ataxie-cerebelleuse, but they are distinguished from the rest of the group as they are from ordinary Friedreich's, by the disturbances of sensibility. Two brothers and one sister.

Tactile sensibility was impaired in all these cases, in some cases analgesia was present, which varied at times and returned. Thus Francois had sensibility to touch and cold abolished below the knee in the year 1892. In the year 1894 there was no affection of sensibility at all, the others were similar. Other cases are reported Stintzing (26) (Munch: Med: Woch: 21 1887), one of Senator's cases, (27), Dejerine (28) mentions a case where a brother and a sister suffered from marked sensory troubles.

#### SUBJECTIVE SENSATIONS.

These are sometimes found. Formication, tingling sensations in the back of the legs and the soles of the feet. Lightening pains have been described. Byrom Bramwell describes a family of three, who had them at one time or another; another with gastric crises, and all from exaggerated sensibility. Charcot had a case with lightening pains. Involuntary spasms have been known to occur. Tressider (29).

*Psychical*  
~~PHYSICAL~~ CONDITIONS.

This is quite normal as a rule and may be expected. In some cases their mental condition is distinctly good. (Tressider, Ladame, Mckenzie (30), Mackey Whyte etc. ) Though cases which are quite normal mentally, at times suffer from explosive laughter and may be easily excited thereto (Ladame). They may at times be a little irritable but as a rule show a high rate of intelligence. Cases have been reported, such as Friedreich's disease with imbecility superadded e. g. Nolan's cases; these are generally speaking the exceptions, and this forms to a certain extent a help in diagnosis, as those cases which are of the "Marie" type are often of feeble mental development. Both the Hardings showed an intelligence rather above the average and far greater than one would expect from looking at them.

REFLEXES.

One may regard the superficial reflexes in Friedreich's ataxia as unimpaired. In both my cases this was so. Plantar, abdominal, cremasteric, etc. were unimpaired, of course one gets variations in reflexes at times just as one may do with patients who are practically normal. Berdez (31) describes a case where the superficial reflexes were exaggerated Besold one where abdominal reflexes were absent. This, however, is not the usual picture, the reflexes being present. The point where this comes in useful is in contrasting the

disease with locomotor ataxia where one sometimes gets loss of the plantar reflex.

#### DEEP REFLEXES.

We will simply mention here the patellar reflex (kneejerk). We may take it as a general rule that in Friedreich's disease kneejerks are lost. To go further, Griffith's in his analysis of 143 cases found it as a very constant symptom: in fact Ladame goes so far as to lay down an absolute rule with regard to it; "that if the kneejerks are present even if the other symptoms are identical with the disease one must mistrust the diagnosis of Friedreich's ataxia." This I think is going too far, as one has undoubted evidence to the contrary; cases though few and certainly rare, do occur. Thus Collier's cases Brain . 1899. There were two cases in which the kneejerks were just obtainable. Tressider's cases also may be quoted where the kneejerk was present in the one and absent in the other. Brock's (32) 2nd. case: a man had kneejerks suffering from ataxia but they were absent in his brother and nephew, ataxics.

Byrom Bramwell has put on record two cases in which the kneejerks were present. Senator in the history of his first case noticed the kneejerks were simply weakened after illness, and again after a considerable lapse of time, a year, the right kneejerk was gone and the left feeble. Erb (33) and Mendel both showed cases with patellar reflexes. Though Erb's may be considered a doubtful case.

In the two cases described before; the kneejerks were quite gone when I examined them though I was a little bit doubtful in the boy's case as there appeared to be a slight tremor on percussion on the left side during the first two examinations. This, however, disappeared in the first fortnight.

#### VISCERAL DISTURBANCES.

These are as a rule quite absent though slowness in the act of micturition has been noted. Griffith's ~~13~~ cases out of 143. In my own cases there was nothing of the kind, unless we perhaps except the attacks of "bilious vertigo" which Wm. Harding suffered from. Twice in three months. Gastric crises have been described in one case (Bramwell).



## PATHOLOGY,

The essential lesions are to be noted in the spinal cord, chiefly sclerosis of the posterior columns of the pyramidal tracts and of the posterior vesicular column in grey matter. It is said that the anterior columns may be affected. The posterior columns are the most deeply sclerosed, involvement of the posterior nerve roots sometimes takes place. The direct cerebellar tracts is affected in some cases, here the sclerosis is a combined one, similar to the ataxic paraplegia described by Gowers. Some of the cranial nuclei are affected at times, notably the restiform body and the posterior pyramidal nucleus. The pia mater over the posterior columns has frequently been described as being thickened. A good many have described the cord as smaller and congenitally imperfect. Some cases present still further evidences of disease; involving Gower's, the mixed ascending tracts in the lateral columns and the column of Turck (direct pyramidal tract). Some meningo-myelitis is to be also seen at times. Practically all these changes occur in the lower part of the tract. I have not had an opportunity of doing an autopsy upon a case of Friedreich's disease. With regard to the post-mortem changes to be found in a case of Friedreich's there is not very much material to draw from. Of all recorded autopsies the number of cases that one can form one's opinion upon are less than thirty of which even some few must be discounted. I will allude in particular to only two. One

of the cases is a post-mortem done and described by Dejerine and Lettulle (46) in "La Medicin Moderne" where the conditions vary a little from other recorded cases. 2ndly. an autopsy done and described by Dr. Mackay upon one described clinically in the American Journal of Medical Sciences (47) vol. cvii 1894 p. 151 and described by him later in Brain. As this is one of the later and more perfect autopsy's done I quote the more important part in extenso.

*Dr. Mackay's case.*

The history of the case.

H. W. Male, unmarried, aetat 23 at the time of examination was one of a family, 3 members of which ( i.e. 2 sisters and himself) had been under observation for some time. A fourth sister had already died from the disease, there was no hereditary transmission of the disease, but various spinal complaints were present in collateral relatives of the patient, and a second cousin probably had died from Friedreich's disease. Had measles and scarletina in his sixth year.

Soon after there appeared weakness of the legs and staggering: at 12 was unable to get about; at 14 his arms were attacked and by his 22nd. year they were helpless.

At the time he presented a typical picture of the disease.

His power of voluntary movement was limited to slight motion at the joints of the upper limbs, raising and rotation of the

head and some control over the muscles of expression. He was also able to roll over in bed, and to raise the trunk on the elbows when supine. His deep and superficial reflexes were abolished: with the exception of normal pupillary reaction to light and accommodation. His sensation was everywhere well preserved and his special senses acute. Coordination had been much impaired before limbs became fixed. He had lateral nystagmus and frequent twitchings in the facial muscles. His speech was laboured and explosive, intelligence was good and he had complete control over his bladder and bowels. The spine showed lateral curvature, optic discs normal. The patient suffered from asthma and cardiac weakness but with no organic mischief. When thirty years of age, he contracted measles for the second time, collapse set in with cyanosis and heart failure under which he speedily sank.

Autopsy was performed 28 hours later. (Permission to open the chest was not obtained)

#### POST-MORTEM.

Cranium	Much adhesion of pachionian bodies.
Membranes.	Normal, no excessive fluid in subdural space,
Brain.	To naked eye, inspection normal, the grey and white matter were natural on section and the convolutions well marked.
Cerebellum.	Well developed, average size and measurements

Medulla. Visibly smaller than normal. Cranial nerves appear normal.

Cord. The dural sac is loose and baggy, and the contained fluid excessive in amount. The latter looks like normal cerebro-spinal fluid. The dura appears thickened, but the pia had no abnormal appearance. The cord is evidently shrunken in size. On section the posterior columns are everywhere greyish and translucent, and the same appearance is visible in the posterior part of the lateral columns. The posterior roots are visibly shrunken in size, the anterior appear normal. Contents of the cranium, spinal cord, and some of the following peripheral nerves viz:- Sciatic R. ant: crural R, ant: tibial L, int: plantar L, R Medial R, Ulnar, L radial, and L post: interosseous were taken for examination. They were hardened in Erlitzky's fluid followed by methylated spirits. The actual changes were as follows:- as seen microscopically.



## CORD.

T. S. Lower Lumbar LV - LIV.

Post: columns.

There is well marked sclerosis most marked in the post: part of the column. At the level of the V lumbar, this involves the post: third of the column. The ant: third next the commissure, shows a large number of well preserved fibres but also a few swollen and degenerate ones. The middle third of the column shows a gradual transition between the conditions described. In the post: third very few stained fibres can be seen and these are scattered at wide intervals throughout the enclosed area. A band of comparatively well preserved fibres lies along the mesial side of the post: horn on each side, separating the sclerosed portion from the grey matter. This, which is continuous with the well preserved fibres lying dorsal to the commissure, evidently represents Marie's cornu-commissural tract. Of the post: R fibres those entering the gelatinous substance ( middle group of Lenhossek) those entering Bordach's column mesial group, and those occupying Lissauer's borderzone, are all intensely degenerated.

The course of individual fibres passing horizontally being marked generally by isolated droplets of myelin; whilst those transversely divided display swollen sheaths and an absence of axis cylinders. The sclerosed area includes the septo-marginal tract of Bruce and Muir and the central oval tract of Fleschig neither of which contain healthy fibres. At the level of L 4 the dark stained fibres occupy only the anterior fourth of the post: column. The remaining  $\frac{3}{4}$  are degenerate, the post: portion most severely. About the centre of the post: column however, a small linear tract of fairly well preserved fibres appeared, bordering on the post: fissure. This has not the oval shape of Fleschig's centrum ovale and probably corresponds to Bruce's septo-marginal tract.

#### Lateral Columns.

At the lower level L 5 there is apparent under the low power of the microscope, a lightening of the myelin stain in a triangular area occupying the posterior part of the column, but separated from the post: horn by the well preserved fibres of the lateral limiting layer. At the higher level L 4 the degeneration is more pronounced and corresponds

with the position of the cross pyramidal tract.

"Marie " holds that the degenerated area in the lateral columns does not represent the cross pyramidal tract" it was noted that the degeneration affected equally the large and small fibres of the area.

It is equally true that many large fibres remained unaffected throughout the tract. The size of the lateral sclerosed area diminished from the mid-dorsal regions upward, but it increased from the lumbar to the mid-dorsal regions, and at the latter level well marked degeneration occurred in the fibres of the direct pyramidal tract, which might account for the lateral diminution from the level upwards. There is distinct neuroglial overgrowth with an increase in the number of round granular glial nuclei..

Anterior columns normal.

Grey matter. post: horn. There is extensive degeneration both of the vertical (ascending) and transverse (entering) fibres in the caput cornu. There is no trace of any healthy nerve cells, while the adjoining large cells of the intermediate grey substance are well preserved: the reticulum of fine medullate fibres in the substance of the horn is fairly but not well preserved.

### Anterior Horn

The large motor cells with their processes and the fibrillar plexus' are well preserved.

### Central Canal.

This is occluded by a mass of small round cells which take on nuclear stains deeply. No trace of ependymal epithelium remains; the post: nerve roots, spinal ganglia, and anterior roots will be described in detail later. It is sufficient here to say that the post: nerve roots are intensely sclerosed. It is unnecessary here to enter minutely into the details of every section of the cord as fully as has been done in the preceeding one.

Sections of the cord were cut at various levels I will just enumerate them

L 1 - D 12

D 7 - D 4

D 2- D 1

C 8 - C 7

C 6 - C 5

C 4 - C 3

L = lumbar D = dorsal C = cervical

### RESUME

Briefly we may classify all the cord changes as follows:- complete sclerosis of Goll's column from the sacral to the upper cervical region, most pronounced in the upper dorsal.



Sclerosis of Burdach's column (only recognizable as such above the level upper dorsal) the degeneration being constant in the portions adjoining Goll's column, and being less marked below in the parts bounding the commissure, and the post: cornua and above the postero-external fields. Sclerosis of Lissauer's tract less marked in the cervical region. Sclerosis of the crossed pyramidal tract from the lumbar regions upwards reaching its maximum at the mid-dorsal level and thereafter diminishing. Sclerosis of the direct pyramidal fibres, from the mid-dorsal regions upwards and increasing from below upwards. Sclerosis of the direct cerebellar tract from the lower dorsal region upwards most marked below. Sclerosis of the post: horns and post: roots throughout. The anterior horns well preserved with the exception of a few cells of the mesial and anterior group, almost total escape of the anterior roots. Complete sclerosis in Clarke's column.

The condition of the nerve roots will now be looked to.

Post: roots in ganglia

These were examined

(a) above the ganglia

(b) in the ganglia

(c) below the ganglia

(b) in the mixed trunks.

The specimens were taken from the lumbar and dorsal regions (sections of the cord in the cervical region for the nerve roots were examined and they showed no difference to those

lower down.)

A. Post: roots between the ganglia and the cords showed extreme degeneration. Staining both by Marchi and Schafer's methods, showed only a very few dark stained tubes of normal calibre present in each root. In the unstained species were seen fine small nerve fibres, empty sheaths and connective tissue. The fine nerve fibres probably the embryonal fibres of Auscher and Dejerine, were frequently closely packed in bundles of from six to twenty fibres. An extremely fine but well stained axis cylinder present in most of them and generally a very thin myelin sheath ( unaffected by reagents). In others ~~the~~, the myelin was disintegrated and granular, and the axis cylinders were sometimes hypertrophied and sometimes absent.

(B) In the ganglia.

Both cells and nerve fibres require to be noticed. The cells and the ganglia appeared smaller than normal, though their longest diameters (when not quite round) gave their average as 50 m, the limits between which they vary being 25 m - 70 m. The average given by Lenhossek being 60 m - 80 m. Pigmentation occurred to a striking extent; in the majority it occupied as much as two-thirds of the whole area of the cell plasma, obscuring the nucleus completely.

(Normal - usually limited to a mass lying between nucleus and thickening ring of plasma, or to a crescentic ring investing nucleus).

It consisted of coarse pigment granules, insusceptible to stain, and agglomerated into dense lumps in which no differentiation of separate granules could be made out.

The cell plasma was invariably opaque and turbid, never highly refractile or translucent. No vacuolation was present but the normal marginal space between cell plasma and capsule, figured and described by Lenhossek, was present.

The nucleoli were well defined in some cases but not in all.

The cell processes could only seldom be detected, the epithelium of the capsules appear normal. In the fasciculi of transversely divided nerve fibres, which appeared on section of the ganglia, there was marked degeneration. Many of the fibres showed granular and disintegrated myelin, and from many the axis cylinders had disappeared. Between these were spaces occupied by fine connective tissue fibres, some apparently healthy some undergoing degeneration, and empty Schwann's sheaths.

Logwood preparations showed a distinct multiplication of connective tissue nuclei, both in the endoneurion between the nerve fibres and in the interstitial tissue between the ganglion cells.

(c) Below the ganglia.

Condition same as described before.

(d) The mixed trunks.

Tr: section showed the two roots lying within the connective tissue sheath apparently much too large for its contents.

In the constituent portions of the nerve in Pal -Weigert and Schaffer preparations: the ant: root showed generally regular and well stained fibres of uniform size, whilst the post: showed a few dark stained discs, and rings in the midst of a mass of unstained sclerotic tissue.

#### The Anterior Roots.

These consisted for the most part of large nerve tubes of 10 - 12m in diameter with healthy sheaths and axis cylinders. They were not wholly free from degenerative changes. This affected chiefly the myelin sheath.

In some cases the myelin had separated from Schwann's membrane and was lying loose in the interior of the tube. In others it was lying in a mass against the inner sheath. In others again the myelin had appeared to have become absorbed, leaving a naked axis cylinder inside the tube so formed.

#### The peripheral nerves.

Those examined were, sciatic in the upper part of the thigh, ulnar, radial, ant: tibial, int: plantar-median and post: interosseus. Each and all showed extreme degeneration. By Schafer's method not only the healthy medullated sheaths, but those also which contained degenerate but unabsorbed myelin gave the black reaction. The unstained areas therefore corresponded to parts which were totally devoid of myelin either healthy or degenerate.



A modification of Sakakya's method was employed in this case for estimating the number of healthy fibres in the fasciculi.

#### Method of estimating nerve degeneration.

"By means of a m. M. Stage micrometer, and a corresponding ruled ocular, the number of healthy fibres present in a series of squares, each with a side measurement of 1 m. m. was counted and an average was taken from nine or sixteen of these squares. Observations on healthy nerve fibres gave thirty-two nerve fibres of 10 - 12m. each in diameter as the average normal contents of such a square. With the normal figure of thirty-two was compared the number of healthy fibres per 1 m. m. square in the best preserved cross section of the nerve. The small fibres, of which large numbers were apparent in all of the peripheral nerves, were excluded from the calculation on account of the difficulty of getting any satisfactory estimate of their normal nerve".

As regards the larger fibres, it was found in the majority of the nerves examined; that is the median, radial, etc. post: interosseus, sciatic, ant: crural, int: plantar occasional fields could still be found where a few squares reached or approximated to the normal contents of fibres.

In the ulnar, and ant: tibial, however not a single field in the cross section of the nerve could an

area containing 32 healthy fibres per 1 m. m. square be found. The relative degree of sclerosis was roughly estimated by measuring the largest superficial area in each nerve in which not a single healthy medullated fibre could be found.

The results may be tabulated as follows: -

In the post: interosseous nerve		
a whole field measuring		contained no healthy fibres
.3 m. m. in diam:		

In the ulnar a space measuring	"	"
.3 x .15 m. m.		

In the radial a space measuring	"	"
.2 x .2m. m.		

In the median a space	"	"
measuring .18 x .18 m. m.		

In ant: tibial .175 x .175 m. m.	"	"
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In int: plantar .75 x .15 m. m.	"	"
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In the sciatic and ant: crural nerves, no sclerotic area larger than .1 m. m. square void of healthy fibres could be found.

Contrary to what one would expect one found that the greatest destruction of nerve fibres took place in the mixed nerves of the upper extremity. In the nerves of the lower extremity it appeared that portions more peripherally placed suffered greater degeneration than those nearer the cord.

Connective tissue hyperplasia was extreme in those fibres in which the sclerosis was most marked and reached its maximum in the internal plantar. In the same nerve the accompanying artery showed an extreme thickening of the intima. The lumen of the vessel being almost obliterated. In the sciatic and ant: crural there was a great deposit of fat in the interfascicular connective tissue. The degeneration was everywhere of the ordinary parenchymatous type, the medullary sheaths being either granular, broken into clumps, or disintegrated with the formation of droplets or absorbed. Persistence of the axis cylinders such as was observed in the anterior roots, was nowhere seen in the peripheral nerves.

#### The Medulla

This was examined at three levels

- (a) Between the pyramidal decussation and the lower level of the olives.
- (b) Lower level of the inferior olive
- (c) Upper level of the olive

(at and above calamus scriptorius)

- (a) Briefly the changes were as follows: - Goll's column (Funiculus Gracilis) completely sclerosed.

Burdach's column (Funiculus Cuneatus) not so completely sclerosed.

Direct cerebellar tract sclerosed.

Gower's tract degenerated.

Numerous degenerated fibres in the direct and crossed pyramidal tracts.

Central canal appears normal. The ependymal lining is distinctly columnar, and outside the epithelial layer is a loosely arranged glial network with Deiter's cells

The fillet layer healthy and well developed

(b) Nothing abnormal of note appears

(c) Fibres gradually getting healthier

Cranial nuclei appear normal xii & x

From the 10th. the medulla shows no marked morbid change

The cerebellum

No signs of degeneration can be found.

The plicae showed a normal arrangement, with a well marked nuclear and numerous healthy Purkinje's cells

I have quoted from this case considerably in extenso as it is not only one of the most recent autopsies of a case of Friedreich's disease but special stress has been laid upon the thorough examination of the peripheral nerves: these have been examined in other cases. I will mention one or two, Guizetti (48) (Riforma Medica June 1893), Mirto's case 49 (Giornale del assoc. del medici. e. naturalisti 1893) Bonnus' case 50 (Nouvelle iconographie de la salpatriere 3. 1898)



In these cases the peripheral nerves showed degenerative changes. In the gross changes most of the autopsies are practically the same and agree in the main with Mackay's case. Dejerine in his autopsy done some years ago and described in *La Medicin Moderne* describes a peculiar whorl-like arrangement of the fibres in the cord, he says "Le sclérose se montre sous forme de tourbillons de fibrilles nevrogliques tassées les unes contre les autres". He says with regard to another transverse section of the cord of the post: columns "fibrilles en faisceaux très longs couches parallèlement à la surface de coupe; les ondulations serpentines des fibrilles donnent à la coupe un aspect des plus remarquables".

The same condition was remarked on by Dr. Bramwell of Cheltenham on a case of his which died and on which an autopsy was held, it was described by him in the *Brit: Med: Journ:* two or three years ago.

#### Double Spinal Canal

Friedreich noted in one of Dr. Omerod's cases (case 6.) that there were in the dorsal regions two spinal canals, one line across; and referred to three other cases in which a double spinal canal extending for a variable distance has been recorded. The condition is extremely rare and it is interesting to note that it occurs in two of these who were at the same time suffering from Friedreich's disease. It is possible that the condition might be caused by connective tissue growing across.



## THEORIES WITH REGARD TO CAUSATION.

Three views are put forward with regard to what may be called the primary degenerative scleroses, Friedreich's disease etc.,

- (1) The Toxine Theory.
- (2) The Senility Theory.
- (3) The Vascular Theory.

(1) The Toxine Theory. As applied to such progressive disease as locomotor ataxia and progressive muscular atrophie. It is thought that in the progressive type of disease, that there must be a poison constantly in the body and constantly acting on diseased tissue. How else can we explain the fact, that an inflammatory process in nervous disease tends on the whole to repair, to limit itself, and to recover; whilst a degenerative process steadily and often speedily tends to progress?. Up to the present bacteriology has failed to discover any microbe, but the fact that many degenerative processes follow infectious fevers and syphilis, has led to the suggestion that pathogenic germs have poured into the system a poison, or have so modified cellular nutrition that there is a poison thrown out which irritates and destroys certain areas of nerve tissues.

## (2) The Senility Theory.

Another view which may be held, is that by the poison of certain infectious organisms the nerve cell is stunned and its growth stunted. Its nutritional equilibrium is destroyed, and premature senility and death are brought about. Just as a man in the full tide of life is made prematurely old by a severe illness or shock and begins to go down hill at the age of 40 instead of at a later age, so the nerve cell and fibre are made unequal to their task and die. In this connection Hirschl speaks of an "agent provocateur". (Wiener clin: Wochenschrift 1896 p. 150) I think that the explanation is not a bad one for Friedreich's disease. In this disease certain strands of the spinal cord were never endowed with vitality enough to carry on their functions for more than a decade or two. Of course the theory of a steadily secreted poison what one may call the Toxine theory is naturally the more hopeful. It is interesting to note in connection with this that degenerative diseases fail to follow those infections which do not confer long immunity, e. g. diphtheria, sepsis, erysepalas, tuberculosis: while the diseases that do confer long immunity such as typhoid, measles, scarletina, smallpox, syphilis, are most likely to set up degenerative changes. Now as immunity is secured through the modification of cell nutrition, or through the continued presence of some antitoxin in the liquor sanguinis of the blood

(Burdon Sanderson Croonian Lect: B. M. J. 1891) it seems not unlikely that the very thing which protects against recurrence of affection may be the cause of some internal degenerative change.

(3) The Vascular Theory.

This is a third theory held by some, and put forward, it is held that the disease is due to a maldevelopment of the blood vessels of the cord. It is not held by many.

The senility theory (premature and artificial if one may so call it), I regret to say is the more plausible one, for it is supported by the fact that certain primary degenerations are started by poisons, for instance lead and ergot have been eliminated from the system. Also by the fact that an inflammatory process may set up a degenerative one, for instance, a chronic polio-myelitis developing into a progressive muscular atrophy.

Is the sclerosis a gliosis?

Alluding more particularly to Friedreich's disease it looks rather like it. Dejerine and Letulle announced that in their case, the sclerosis in Friedreich's ataxia was a gliosis and so differed from other scleroses. They pinned their faith and based their observations on the reactions obtained by Malassez's histo-chemical process.



## Malassez's test.

## Process -

The sections are placed for 10 minutes in a 40% solution of caustic potash, then washed and stained with carmine, placed in crystallised acetic acid washed and mounted in acid glycerine. The connective tissue is softened and partly dissolved and does not take up the carmine stain, while the glial tissue is not injured, and is stained.

Of course they pinned their faith to the test.

Melassez himself is rather doubtful, but still they have a good deal of probability on their side. Therapeutically the theory may have some value, as it is a curious thing that arsenic and silver <sup>which</sup> have a distinct value in treating some of these scleroses, have no value in fibroid processes elsewhere; and are known to effect epiblastic rather than mesoblastic tissue.

To refer back for a moment to the case of Dr. Mackay might be useful. The extreme preponderance of the degeneration in post: roots rather than the anterior indicates that it is the afferent fibres of the peripheral nerves that are principally affected. Still the fact frequently recorded, that the patient's sensibility to touch, pain, and temperature remain unimpaired throughout, suggests that it is the afferent nerves from muscles that chiefly suffer.

Guizetti came to this conclusion, he thought that in his case there existed a systematic atrophy of sensory fibres.

He in his case considered, however, that muscular and cutaneous fibres were both affected, and it should be remembered that clinically the patient's tactile and thermic sensibility were diminished below the knees, and that there was some tactile impairment present in the hands. If one refers back to the autopsy of Mackay's case there were one or two slight abnormalities occurring in the dorsal and cervical portions of the cord which were suggestive of structural anomaly dating back to the developmental period of the cord. Sections containing these abnormalities were variously stained, to try and ascertain their finer structure. The nerve fibres traversing the areas were invariably degenerated, and none possessed axis cylinders. The intervening ground substance resembled closely the sclerotic tissue present in the post: parts of Goll's column, and was so dense that it could hardly be examined. However, though the Deiter's cells could not be made out clearly, the corpora amylacea were present in considerable numbers. The staining reactions were those of glial tissue, and in all probability the structure was that of a circumscribed gliomatous mass of long standing, in which the cellular elements seemed to have disappeared.

No appearance corresponding to Dejerine's description of whorls of glial tissue could be seen. The grey sclerotic area in the post: and lateral columns were found histologically to have the structure of neuroglial hyperplasia

elsewhere. Numerous large Deiter's cells were present. These cells were less distinct and stained less freely in the older and more completely sclerosed portions, while they stained most distinctly in the transition zone between healthy and degenerating tissue. Where they stained least distinctly in, for instance, the peripheral portions of the post: columns, there the corpora amylacea were seen in great numbers; and were least distinct where the glial cells were most prominent. (I refer to this case again as it is interesting to take the conditions into review when considering the theory that the sclerosis is a gliosis) furthermore the vessels were nowhere markedly thickened but everywhere distended with blood. Furthermore contrast this latter fact with the theory of the vascular causation of this disease held by Pitt (51), Blocq, and Marinesco (52).

These observers all found changes in the vessels of the post: columns; also Schultze (2nd. case) and Everett Smith.

Against them one may put the cases of Rütimeyer, Dejerine and Letulle, Guizetti and Mackay's case before mentioned.

For some other reasons against the vascular theory Guizetti points out

- (a) That disease of the post: vascular system would leave unexplained the condition of the post: roots and spinal ganglia.
- (b) That Clarke's column, which is generally, in fact, always sclerosed, is supplied by the anterior system of vessels.

- (c) That such vascular dilations, described by Pitt, Blocq, and Marinesco are of frequent accompaniment to sclerosis of the cord and are no doubt secondary to it.

I do not think that we can do better with our present knowledge of the pathogenesis than to sum up, "That Friedreich's disease depends upon a congenital predisposition, in consequence of which in the early years of life, certain systems of fibres and nerve cells undergo a process of progressive atrophy; and that the process is independent of any contributory effect from vascular degeneration."

To be more exact in alluding to "certain systems of fibres and cells" we understand the following -

- (1) (due to arrested development at the eighth month)  
Tracts in the cord which are the latest to undergo medullation namely: - the pyramidal tracts direct and crossed, and the postero-internal tract.

- (2) (Secondary to maldevelopment Goll's column)  
The system of fibres and cells functionally related to the postero-internal tract. The extent of the atrophic process as to systems attacked, and degree of degeneration in individual systems may be dependent upon the duration of the disease.

These systems may include: -

- (a) The peripheral sensory neuron, complex in its entirety, namely:- peripheral sensory fibres ganglion cells, post: roots and root zones (Burdach's, Lissauer).



fibres to Clarke's columns, to the middle zone, and to the anterior cornua.

- (b) Portions of the central sensory neurons, namely cells in the post: horns, with associated ascending fibres, cells in Clarke's column with associated fibres (direct cerebellar tracts), cells in the middle zone, with associated fibres (Gower's tract), cells in medullary nuclei, clavate and cuneate, with associated fibres (internal arduate).

#### THE ORDER IN WHICH THE SYMPTOMS APPEAR, METHOD OF ADVANCE AND PERIOD OF ONSET.

This is a difficult matter to settle, but as it is generally their method of walking; or the fact of the mother noticing that the child walks badly in the first place (being frequently brought to the hospital for this symptom alone)

I think we may take it that ataxia of the legs was the first symptom.

In both my own cases this was the first symptom, and in several other cases I have had the opportunity of seeing it was the first prominent early symptom. In other cases the first symptoms were as follows:- Griffiths in his analysis (International Journ: of Med: Sci: Oct: 1888)

Lower extremities attacked first 114 cases.

Upper extremities 10 cases

Arms and speech simultaneously 8 cases

Legs and speech first attacked 2 cases

Arms alone 2 cases.

Arms first affected in (Besold's case)

Arms first affected in Mendel's case.

Spinal curvature first noticed in James' (34) case. This was also the first symptom noticed in one of Brock's cases.

Thus I take it we may consider that in the majority of cases, the ataxia of the legs is the first symptom, then the disease appears to mount higher until finally ataxia of the arms takes place, then further affections of the speech are observed.

The average lapse of time, however, before the upper extremities become ataxic is six years. As far as we can rely on statistics this seems to be about the time but still there are cases where the interval may be long, 20 years, (Dreschfield's case), or 17 years (Griffiths' case ).

Ataxic movements of the head and trunk may appear with the ataxia of the arms, or may appear later. The appearance of bulbar affections, the affection of speech being generally the first, averages only one year and a half after the incoordination of the arms appears.

In 18 out of 21 cases both cases appeared simultaneously.

As the disease advances more or less paralysis, muscular

atrophy, talipes, contractures of the feet, curvatures of the spine and perhaps sensory affections, come on.

The patient eventually becomes completely crippled and unable to walk. These patients may die from asthenia, this is not common as they generally die from "intercurrent disease".

But cases vary tremendously in character; some cases may remain in statu quo for some considerable time, for instance case 1., while others go from bad to worse very rapidly such as case 2. With regard to the time when the disease commences there is a good deal of diverse opinion.

Friedreich himself considered it to be a disease of puberty (e. g. one of the facts for the vascular theory).

I think that after looking through a great number of cases, you will not be very far wrong in putting the onset of the disease generally speaking as occurring between the ages of 6-9, most common 7th. - 8th. year. (Gowers) Out of the 147 cases analysed by Griffiths 25% occurred before 6 years of age and over 50% before 11 years. In 15 cases the disease began in infancy, and in not more than 25 did it develop after 16. In fact it is very unusual to find the disease developing after 16 years of age. In those cases, which are said to occur after this age, might it not be due to the fact that as the symptoms are so imperceptible and it may be two or three years before any marked symptoms are noticed, that in these cases the disease

has really started before that age? Auscher puts on record a very late case at the age of 25, but the case is open to grave doubt.\* Charcot puts on record two cases one 25 and the other 21 years respectively. An interesting fact in connection with the starting age of this disease in a family, is quoted by Soca, he enunciates the opinion that "Friedreich's ataxia almost always begins at or about the same age in a family or within a year or two of that year."

This is important with regards prognosis, as he says that a child which escapes the critical year will probably escape altogether. This, however, is not born out by facts. Take Byrom Bramwell's cases affected  $6\frac{1}{2}$   $5\frac{1}{2}$  6 years, again 14 18. Mackay Whyte's cases affected 11, 7, 15, years, my own cases affected at 7 and 8 respectively.

However, there is one thing we may agree upon in conclusion after going over these statistics, that the disease is one of a developmental period.



THE DIFFERENTIAL DIAGNOSIS  
OF FRIEDREICH'S DISEASE FROM OTHER DISEASES  
WHICH IT SIMULATES.

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These are Locomotor Ataxia, Marie's type of hered: cerebellar ataxia, chorea, ataxic paraplegia, and cerebellar disease.

The diagnosis of a case of Friedreich's disease if an isolated one is apt to present a good many difficulties, but if one comes across a series of cases of the family type as a rule with a little care, one will not have much hesitation in referring them to their proper positions. As the great wealth of clinical material accumulates from year to year, one is continually coming across groups of cases, which though of a familial character present slight but often significant differences from true Friedreich's disease; notably we may take Nolan's (35) cases of three with mental imbecility, Sanger Brown's (36) series of cases, of which he described 100 (unselected). This latter class I have thought right to discuss separately under the heading of Marie's type, as they form a very important class. To resume our discussion of the diagnosis, Friedreich's disease is essentially one of the family types of nervous disease like pseudo-hypertrophic disease, and Thomsen's disease. Isolated cases do occur and it is sometimes difficult to refer them for this reason to their proper place. In some cases even after an autopsy one would hesitate to put them into the class we are speaking about. I allude to the cases of Tedeschi (37),

Dana (38), T. S. Wilson cases 3 and 4 (39.)

The differential diagnosis between this disease and locomotor ataxia.

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Locomotor ataxia is much more a disease of the adult, and attacks men more often than women, Friedreich's is a disease of early life and is as common among girls as boys. Friedreich's is a disease which attacks the imperfectly developed and congenitally imperfect cord; locomotor ataxia is one that attacks the fully developed and structurally healthy cord. Locomotor ataxia is very rarely developed before twenty, when it does so all the symptoms are particularly severe, and the clinical picture very apparent (Charcot). It is rare, it is doubtful if it is ever met with before sixteen. Friedreich's disease develops before the age of twenty and generally about seven years of age or at the time of puberty. Any variation from either of these dates in either disease is rare. In locomotor ataxia, we have no family type, in fact it is quite exceptional to have two cases of the same family affected with ordinary tabes. With regard to the history, syphilis is frequently found in tabetic people, but there is no evidence that it is one of the factors in producing Friedreich's ataxia. Lightning pains if present, and they have been described in Friedreich's disease (Bramwell) are very rare, they are common in tabes. There is a very long pre-ataxic stage in tabes presenting the most diverse symptoms namely - ocular, visceral, etc. changes. No preataxic stage is to be observed in a similar way in Friedreich's

ataxia, but a condition simulating chorea is present often for several years. In Friedreich's ataxia, there is ataxy during rest and movement, choreiform instability present, movements inco-ordinate feeble and not as a rule sudden. Ataxy general, its progress from below upwards. The gait is cerebellar in type, ataxic as well (festinating). Closure of eyes causing loss of equilibrium by reason of the general instability, due to a static ataxia. Contrast this picture with the following one of tabes dorsalis. Ataxy during movement. At rest the patient is quiet. Ataxic movements are sudden, as if the patient was set on springs. The tabes may be localised in the arms or legs (cervical tabes) gait characteristic and stamping. The patient can walk in a straight line, closure of the eyes causes loss of equilibrium, because it takes away the knowledge of the position of the limbs (Romberg's sign).

In Friedreich's disease there is usually integrity of sensation until at any rate a late stage of the disease. The knee reflexes are generally absent, but the plantar reflexes are generally present. In tabes there is great perversion of sensation frequently, lost kneejerks, and the plantar reflexes are usually absent. In Friedreich's we have as a rule no affection of special organs. Nystagmus is usually present, there are very rarely affections of the eye, and there is absence of visceral affections. In tabes frequent affections of the eye occur, grey in-duration of the optic nerve, amaurosis, sclerosis of the auditory nerve, myosis, Argyle Robertson pupils

diplopia, ptosis. There is very rarely nystagmus. You sometimes have crises occurring, laryngeal, (Spasm of the glottis), gastric, intestinal, anal, vesical, and nephritic.

In Friedreich's;

You have no lesions of the bones, skin or joints. You have a characteristic form of the club foot, contractures, and sometimes athetosis of the toes. No peripheral neuritis.

In tabes;

The changes one may meet with are many and various. Cutaneous and trophic lesions. Muscular atrophies, perforating ulcer of the foot. Peripheral neurites, sensory and motor (common) are met with.

In Friedreich's;

You have no trouble with the integrity of the sphincters. There is scoliosis. Speech is slow, slurring and scanned. There is progressive uniform development of the disease.

In tabes;

You have frequent vesical and urino-genitary troubles. The sphincters are not always good. No scoliosis. Speech is good. Sometimes the disease is very rapid after a bad crisis.

I think that on contrasting these symptoms that one will not have much trouble in diagnosing between the two diseases



The differential diagnosis between Marie's type of case and  
Friedreich's.

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The disease which has been called by some Marie's disease, has on more than one occasion been confused with Friedreich's. Its name has been given to it to illustrate three important facts (heredo-ataxie-cerebelleuse)

1. That it is a family disease.
2. That ataxy or at least the staggering gait known as cerebellar ataxie, is a leading symptom.
3. That the lesion is in the cerebellum.

This last fact distinguished it from Friedreich's disease, where there is family ataxie present but in this case it is spinal. Yet the two diseases are closely related; both consist of a cerebo-spinal degeneration beginning in the one case in the cerebellum (Marie), and in the other in the cord (Friedreich). One case has been described where the two diseases apparently co-existed, both cerebellum and spinal cord were degenerated. (Menzel).

Marie.	Friedreich.
Family disease	Family disease.
Usually noticed after 20.	Usually noticed before 20.
This may explain why it appears in successive generations.	Generally too young so skips a generation.

Marie.

Friedreich's.

As the patients are of  
marriageable age before  
the disease appears.

Family history similar

Family history ditto.

Parental alcoholism

both have spinal symptoms,

do.

ataxic gait, absence of  
sensory symptoms, at least  
in the early stage,

do.

affection of speech.

do.

Irregular choreiform  
movements.

do.

Thus one can see there are a good many points of resemblance.

The points of difference are as follows: -

The movements are very exaggerated compared to the twitchings and general unsteadiness of Friedreich's disease. The explosive speech of Marie's affection differs very much from the drawling imperfect articulation of Friedreich's disease. In Marie's cases the tendon reactions are exaggerated even in the early stage (showing primary disease of the lateral columns.)

Contractures also are setting in (Sanger Brown). In Friedreich's the tendon reactions in the great majority are gone quite early, contracture may exist, though in a subsidiary form for the morbid anatomy was always shown that sclerosis of the post:

columns is always greater than <sup>of the</sup> lateral in this disease. In Marie's disease there is no nystagmus but, Sanger Brown describes a peculiar action of the levatores palpebrarum, Ophthalmoplegia, and optic atrophy in his cases. These are quite unknown in Friedreich's.

There are several groups of cases which bear a superficial resemblance to Friedreich's disease, <sup>which</sup> with much more reason might be assigned to Marie's class. These are the series of cases collected by

1. Sanger Brown. He publishes two lots, one a series of 100 cases, and another a series of twenty-one selected cases with no autopsy.
2. Dr. Nonne (40); publishes cases of the Stube family with one autopsy. At this autopsy was found smallness of the nerve centres, cerebrum cerebellum, pons, medulla and cord. Atrophy accompanied without any inflammatory change therefore he considered it to be primary and dependent on defective development. No degeneration of the spinal tracts was found, atrophy of the optic nerves was the only sign of positive degeneration.
3. Menzel. The case before mentioned.

Dr. Sanger Brown as before mentioned published a list of 24 cases in "Brain" and he claims that they belong to Friedreich's class. It will be worth while to consider for a moment these cases as a whole in relation to Friedreich's disease.

1. Broadly, the principal symptoms of this class were "Ataxia of the limbs", Usually beginning in the legs and progressing upwards, rendering the patient in time helpless, though muscular power present.
2. Excess of tendon reactions.
3. Contractures of tendons.
4. Ankle clonus.
5. Skin reflexes exaggerated.
6. No sensory symptoms ( exceptionally pain).
7. Articulation was interfered with ( apparently due to uncontrollable muscular action), a tendency to choke when swallowing.
8. Drooping of the lids like ptosis, but when looking, over-action of the levatores palpebrarum takes place, and the eyes stare
9. Vision fails, often early, from progressive optic atrophy. Pupillary action to light defective, probably due to optic atrophy.

Later "As the disease progresses extensive choreiform movements of the head and often of the arm accompany all voluntary movement".

"Then irregular movements occur in the hands, legs, and head, whenever it is attempted to maintain either of these parts in a fixed position by voluntary effort."

There is a family resemblance in all his cases and the onset of symptoms is late, most frequently between the ages of 16 to 35 but it may be as early as 11 and as late as 45.



One has simply to run over the main points of Friedreich's disease, and one sees at once the great difference between these two classes of cases. The fact of no autopsy having been done on any of Sanger Brown's cases leaves the matter a little doubtful. Still I think that all things considered they approximate more to Marie's type, in which we also place the Stube family of Dr. Nonne.

Briefly we may sum up

Sanger Brown's Cases.	Friedreich's disease.
Late onset, as late as 45.	Early onset 6 to 18.
The majority of his cases do not happen in female sex (only carrying over).	
Frequent ptosis	Absent.
Nystagmus not general.	General.
Ambylopia, amaurosis, constant.	Not present.
and early symptoms. Kneejerks increased.	Kneejerks diminished.
Foot clonus. No club-foot or scoliosis, pupil reactions deficient	Foot clonus absent Club-foot and scoliosis present.
(due to optic atrophy)	Does not occur.

The differential diagnosis between chorea and Friedreich's ataxia.

The diagnosis here can present no real difficulty, as it is only in the very recent stages that the diagnosis can be confounded. There are, however, on record, at least two cases where undoubted cases of Friedreich's ataxia were treated as chorea (Moxon, Omerod) (41), Ladame, Bramwell also. T. S. Wilson's case 4 said to be a case of Friedreich's disease which was sent to hospital as a case of chorea appears simply to have been a bad case of this disease.

History of the case.

The picture drawn seems clear enough for chorea. "The unsteadiness became so marked that in a fortnight from onset the least thing would knock him down. There was muscular weakness, lordosis, increased kneejerks, spastic tendency. Much improvement in hospital. Whole duration of illness eight months." This reads uncommonly like a bad case of chorea. Diagnosing between the two, stress must be laid on, the movements of the tongue, the face movements whether unilateral or not. The face movements may occur in Friedreich's ataxia. The tongue is protruded and jerked up and down in chorea; in Friedreich's disease there is shown an irregular tremor, no jerks. The ataxia of course if marked, gives one the clue at once; so, it is really only in the early stages that the diagnosis is doubtful. Chorea does occur in families, family tendency is sometimes marked, though the proportion is not great. (Gowers).

The feet and kneejerks will also afford a valuable evidence. Huntington's chorea is hereditary, it occurs in adults, is rapidly fatal and the patients are mentally affected.

The differential diagnosis between cerebellar disease and  
Friedreich's ataxia.

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The symptoms are as follows: - Reeling gait of a zig-zag character, difficulty in standing, Nystagmus, sometimes the patellar reflexes gone. The gait is not tabetic in character, and there are probably no jerky choreiform movements. The arms are usually steady, rarely they present some jerky in-coordination (Gowers), If there is a tumour probably pressure symptoms would be present or come on in time. There is sometimes a great general resemblance to Friedreich's ataxia, but on carefully weighing up the symptoms it is extremely improbable that real difficulty will be found in the diagnosis.

between

The differential diagnosis, ataxic paraplegia or the combined postero-lateral sclerosis of adults and Friedreich's ataxia.

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The diagnosis here is also fairly easy in a typical case. This disease seldom if ever begins in childhood, it affects males much more frequently than females, and it usually develops between the ages of 30 and 45. The cases are generally isolated ones: and there sometimes appears to be a neurotic family history. Here we have the kneejerks increased, though they

may be absent in the later stages, especially when the disease has progressed somewhat. Ankle clonus is frequently present. The motor powers of the lower extremity are impaired, even early. The gait is quite unlike Friedreich's. The upper extremities usually escape. Bladder and rectum are frequently affected. Sexual power is often impaired. Dull pain in the back sometimes. No foot deformity, scoliosis or nystagmus occur. Speech generally good, the choreiform movements seen in Friedreich's not usually observed.

Perhaps it would be as well to run over various points of difference between Friedreich's disease and disseminated sclerosis. Marie, Unger (42), D'Espine (43), have all put on record cases of this disease in children, so it may be as well to consider the main points briefly.

In disseminating sclerosis the tremor is coarse and jerky, the nystagmus is much more noticeable and the tendon reflexes are more exaggerated. Ocular paralyses and affections of the optic nerve are frequent, but the disease fluctuates a great deal. The gait at times may be cerebellar in type and not spastic, the kneejerks may be absent, scoliosis may be present, and the speech instead of being scanned may be like that of Friedreich's. But, all the apoplectiform and epileptiform ~~attacks~~, vesical paralyses, trophic and mental disturbances are wanting in Friedreich's disease.



The general expression of the authors quoted before is that in children, the disseminated sclerosis most often presents the cerebro spinal type which commences by convulsions.

There are of course several other combined sclerosis which have been described by Bouchard (44), Ewart (45). Other types are the ataxo-spastic tabes of Grasset, spastic-tabes dorsalis (Erb, Charcot, Strumpell), and the anomalous types described by Oppenheim. But we will not discuss these types as it is comparatively easy to build up a group of symptoms with the diseases we have considered. After a consideration of these different diagnosis I think that in a fairly well marked typical case of Friedreich's disease one could be certain of ones diagnosis. Naturally the great difficulty will be found in regard to the isolated cases. But even here if care is taken to look at the main symptoms little difficulty will be found.

Friedreich's ataxia is a rare disease and naturally enough is only comparatively well known to the neurologist; this too adds a certain amount of difficulty to the diagnosis, unless the physician be on his guard for the isolated type.

## THERAPEUSIS.

Very little apparently can be done for these cases, therapeutically we have no remedy that has a specific action. Silver, arsenic, phosphorus, zinc, strychnine, iron, cod-liver oil etc., all appear to have been tried by most writers and all agree that no very great benefit is to be obtained from their use; though most writers speak very favourably of the cod-liver oil. Personally I think I found that the patient seemed better when taking arsenic ~~than~~ cod-liver oil. I tried them with all remedies before mentioned and the latter I think were the most useful, probably because their general health was better. The battery was used in case 2 the sister, she said she felt better after it, but it was a question if she improved at all. The brother said he felt worse after it. Massage was tried in both cases, but without any success. A poroplastic jacket has been recommended by some writers; (Everett Smith, and Griffiths). and improvement is said to have taken place. Suspension has been tried in some cases (Bramwell) without any lasting improvement. It has been found that by means of combined exercises, these patients can be made very much more useful to themselves and others; but as to whether there is any real improvement or not must remain open to doubt.

## PROGNOSIS.

The disease tends to steady and continuous progress in a downward course, without any period of marked improvement. It ultimately ends in death, and though this may be from asthenia is generally from intercurrent disease. The duration of illness may be lengthy, twenty or thirty years, but, in the later stages the patients are generally very helpless.

Finis.

## Note.

A Bibliography is appended of various authors, from whose works I have quoted; an appendix with three interesting family charts is also added.

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# Genealogical Table of the Vitielli Family,

(Reported by Vizioli (2) Giornale

## Father

Aniello Vitielli

Died at the age of 75 of cerebral apoplexy  
Gouty but healthy, strong up to the moment  
of his death, a drinker of wine, lively disposition  
passionate

16 children of whom three only were healthy 8

1.	2.	3.	4.	5.	6.	7.	8.
Marianne Left fa - cial congenital	Guisepe died aet 3	Rosa ataxic aged 26 had never walked Paralysis of all four limbs. Speech affected	Raffaello died aged 10 months	Guisepe ataxic died aged 16 of cerebral hemipgia general motor power great Curvature of Spine.	Antonio Hypochondriac died aet 40 of anaemia	Vincenzo ataxic Paralysis of legs speech affection,  married had 5 children 2 of whom were ataxic, the disease developing at the age of 2 & 3 years when they began to walk. Of the three remaining children 2 suf- fered from sleep- lessness & 1 who was healthy died at the age of 6 of scarletina	Raffaello irascible

affected with Friedreich's ataxia

di Neuropatologia 1885 p. 15)

Mother

Luigia Luisi

Died at the age of 72 of dry gangrene. Several convulsive attacks during youth, affected with megrine all her life, of an original odd disposition

( 4 males 4 females ) ataxic two grand children, young infants their father ataxic

9.	10.	11.	12.	13.	14.	15.	16.
Aniello drank hard	Lucia irritable married no children	Fitomene ataxic in all four limbs Lower ex- tremities paralysed and atrophied married no children	Margarhita ataxic in all four limbs Speech affected married 3 healthy children did not suckle them	Andrea ataxic in all four limbs skeleton and limbs poorly de- veloped married 2 healthy children	Maria ataxic paralysis & atrophy of the lower extremities.	Luigi aged 30 years healthy nothing abnormal	Francisco ataxic never walked died aged 6 of an in- tercurrent ailment.



Rutimeyer ( 7) has reported a very remarkable series of cases which occurred in a family named Blattner the great- great - great grandfather of the present generation who married in 1710, was in all probability affected with the disease, for he was nicknamed "the stumbler", he states that all the direct descendants of the Blattner ( the great-great-great-grandfather of the cases of Friedreich's disease) are inscribed under the surname of Stumbler (Stützi) in the official registers of the Commune of Kuttigen (Argovie) until the year 1840; he also remarks that the gait of this man must have made a great impression upon his contemporaries, since it remained for so many generations in the memory of the inhabitants of the country.

Genealogical Table of the Blattner Family, affected with Friedreich's ataxia

(reported by Rutimeyer in Vichows Archives vol. xci p. 116)

Blattner (nicknamed the Stumbler) presumably ataxic the great great - great - grandfather of the ataxic patient

married in the year 1710

1.	2.	3.	4.
Blattner - Blattner	Blattner -Kyburg	Blattner-	Blattner-Basler
10 children, of whom	7 children	Wehrli	7 children of
7 were healthy 3	of whom 6 were	10 children	whom 6 were
were ataxic Rudolph (1)	healthy, 1	of whom 7	healthy and 1
born 1865 ataxic after	ataxic Rudolph (2)	were healthy	ataxic, Karl
scarlet fever Gottlieb	born 1867	3 diseased	ataxic, his
born 1848 ataxic Marie	typhus fever	Marie Madeline	mother was af-
born 1853 ataxic		20 years ataxic	fected with
		Fritz, died of	chorea in
		measles at the	childhood;
		age of 9 ataxic	a paternal uncle
			became suddenly
			paralysed in both legs
			(acute polio-myelitis. )

(From Ladame's Monograph)

Genealogical Table of the Family of Marchis-Rivotti affected with Friedreich's disease  
Reported by Musso (6)(Rivista clinica di Bologna. 1884. p. 865.)

Marchis-Rivotti Antionia

Melancholia, passing into dementia

Ignazio

Catterina

Healthy but nervous, and of feeble constitution  
his wife healthy.

Wife of Dardino Guiseppe, both healthy

Antonio Anna Dead Maria Giovanni - 7 children  
ataxia ataxia born ataxic healthy

Maria Bernardo Antonio Domenico Magdalena Angelo Deadborn Ignazio Antonio Giovanni Deadborn.  
Ataxic Ataxic  
died aged 40  
ataxic  
aet 45.

13 children  
First Cousins

Nota Bene

The three male ataxics were descended from the grandfather, affected with dementia  
thro' the female line  
The three female ataxics were descended from the grandmother affected with melancholia  
thro' the male line.